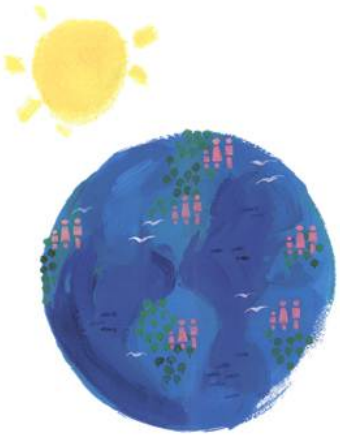
NICEATM

National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods

ICCVAM

Interagency Coordinating Committee on the Validation of Alternative Methods



Overview of the ICCVAM Workshop on Best Practices for Assessing the Potential for Chemically Induced Eye Injuries

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CDER, FDA, OTWG Chair

SACATM Meeting

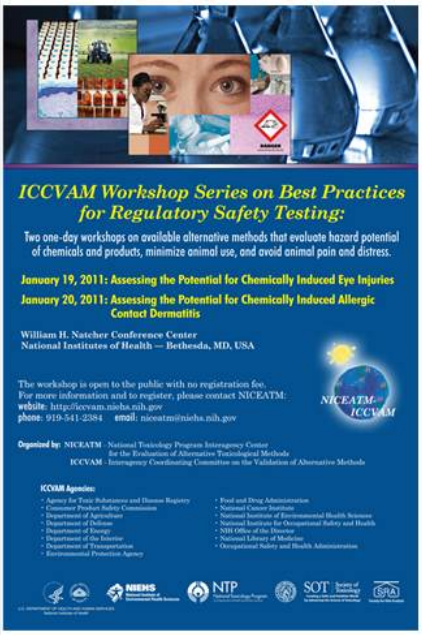
June 16, 2011

Hilton Arlington
Arlington, VA

National Toxicology Program

NIEHS

Best Practices for Regulatory Safety Testing: Ocular Safety Testing Workshop



- NIH – William H. Natcher Center, Bethesda, MD
- January 19: Ocular safety testing
  - 77 participants
  - Mostly government and industry participants
  - Equal representation
- Poster session
  - 16 ocular posters

Pre-workshop Communications Efforts

- FR Notice (Oct. 13)
- Six announcements sent to ICCVAM email list (958 individuals)
  - Requests to "spread the word" also sent to 12 additional industry contacts not on ICCVAM email list
- Articles in regular NICEATM updates to NTP and ALTEX
- Requests to post on websites sent to 25 organizations
  - 15 actually confirmed posted
- Posters sent to EPA, CPSC, FDA via ICCVAM reps
- SOT and SRA co-sponsorship
  - Email announcement to full SOT membership
- Also supplementary emails to relevant SOT specialty sections

NIH Center for Information Technology Webcast

- Live webcast of workshop
  - Over 90 online viewers each day
- Webcast included all plenary sessions

- Archived webcast available at:
  - NIH Videocast page http://videocast.nih.gov/PastEvents.asp
  - NICEATM-ICCVAM website http://iccvam.niehs.nih.gov/meetings/Implement-2011/ImplmtnWksp.htm

Summary of Program: Ocular Safety Testing Methods Workshop

- Introduction/Public Health Impact
- Available Test Methods
  - Eliminating pain and distress during *in vivo* ocular safety testing
  - Bovine Corneal Opacity and Permeability (BCOP)
  - Isolated Chicken Eye (ICE)
  - Cytosensor Microphysiometer (CM)
- U.S. Requirements for Consideration of Alternatives
- Current Guidelines for Safety Testing
- Regulatory Agency Roundtable Discussion
  - EPA
  - FDA
  - CPSC
  - OSHA
- Case Studies
  - Breakout groups
  - Summary presentations

Ocular Safety Test Methods Discussed (1)

- Pain Management/Humane Endpoints in *In Vivo* Testing
  - Routine use of topical anesthetics and systemic analgesics using ICCVAM-recommended procedures
  - Humane endpoints to terminate a study
- BCOP Test Method
  - Current validation status - identification of severe eye irritants/corrosives (OECD TG 437)
  - Application, controls, protocol details, scoring, calculations, and prediction model
- ICE Test Method
  - Current validation status - identification of severe eye irritants/corrosives (OECD TG 438)
  - Application, controls, protocol details, scoring, calculations, and prediction model

Ocular Safety Test Methods Discussed (2)

- Cytosensor Microphysiometer Test Method
  - Current validation status
    - Identification of severe irritants/corrosives (water-soluble surfactants or surfactant formulations and nonsurfactants
    - Identification of substances not labeled as irritants (water-soluble surfactants or surfactant formulations **but not pesticides or nonsurfactants**)
  - Application, controls, protocol details, scoring, calculations, and prediction model

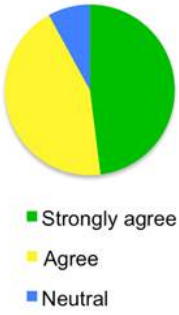
New Ocular Safety Testing Methods in the Validation Pipeline

- ECVAM Eye Irritation Validation Study (EIVS)
  - Epi-Ocular™
  - SkinEthic™
- Other Non-animal Test Methods and Strategies
  - Fluorescein leakage test method
  - Antimicrobial Cleaning Product testing strategy pilot program
  - Isolated rabbit eye test method
- JaCVAM 2nd Validation Study
  - Short time exposure test method (STE)

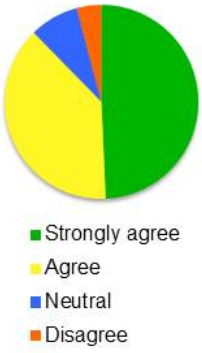
Survey responses: Ocular Workshop

- Number of surveys received: 26
  - Total attendance: 77
- Respondents:

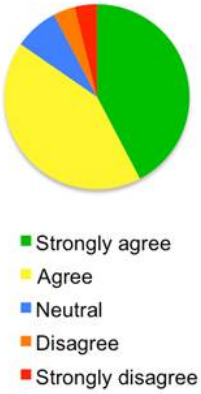
Were satisfied with the workshop and the information presented



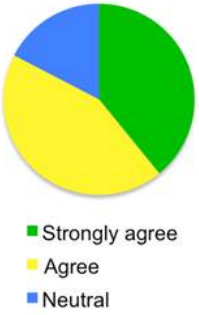
Felt that the workshop achieved each of its stated goals*



Felt the presentations were useful and practical*



Felt the posters were informative and relevant



*Represents a summary of data from several questions

Case Studies Overview

- Four ocular case studies were presented to highlight:
  - The potential for reducing animal use by using the BCOP, ICE, and CM in vitro test methods
  - How to conduct and interpret results from the validated in vitro ocular test methods
    - BCOP
    - ICE
    - CM

Case Study Summaries (1)

- Use and interpretation of BCOP test method results
  - Describes the tiered-testing strategy to be followed to determine whether a validated and accepted *in vitro* ocular test method should be considered (TG 405; OECD 2002)
  - Positive BCOP results can be used to classify certain substances as ocular corrosives and severe irritants without further testing (TG 437; OECD 2009)

Case Study Summaries (2)

- Use and interpretation of CM test method results
  - Positive CM results can be used to classify water-soluble surfactant chemicals and certain types of surfactant-containing formulations as substances not classified as ocular hazards without further testing (ICCVAM 2010)[1]
    - First *in vitro* test method to be recommended by ICCVAM for this testing purpose

Case Study Summaries (3)

- Use and interpretation of ICE test method results
  - Positive ICE results can be used to classify certain substances as ocular corrosives and severe irritants without further testing (TG 438; OECD 2009)
  - Ketones are an identified limitation for the BCOP test method
  - Pain management procedures that should *always* be used when it is determined necessary to conduct the rabbit eye test (ICCVAM 2010)[1]

Case Study Summaries (4)

- Use and interpretation of CM test method results
  - Positive CM results can be used to classify water-soluble surfactants, surfactant-containing formulations, and **nonsurfactants** as ocular corrosives and severe irritants without further testing (ICCVAM 2010)
  - Alcohols are an identified limitation for both the BCOP and ICE; CM provides an *in vitro* option for some of these substances

Acknowledgements

- Society of Toxicology (Co-sponsor)
- Society for Risk Analysis (Co-sponsor)
- ICCVAM
- ICCVAM Ocular Toxicity Working Group
- NICEATM Staff